A NORMAL DISTRIBUTION FOR TENSOR-VALUED RANDOM VARIABLES TO ANALYZE DIFFUSION TENSOR MRI DATA

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ABSTRACT

Diffusion Tensor MRI (DT-MRI) provides a statistical estimate of a symmetric 2nd-order diffusion tensor, $\boldsymbol{D}$, for each voxel within an imaging volume. We propose a new normal distribution, $p(\boldsymbol{D}) \sim \exp(-1/2\ \boldsymbol{D}{:}\boldsymbol{A}{:}\boldsymbol{D})$, for a *tensor* random variable, $\boldsymbol{D}$. The scalar invariant, $\boldsymbol{D}{:}\boldsymbol{A}{:}\boldsymbol{D}$, is the contraction of a positive definite symmetric 4th-order precision tensor, $\boldsymbol{A}$, and $\boldsymbol{D}$. A formal correspondence is established between $\boldsymbol{D}{:}\boldsymbol{A}{:}\boldsymbol{D}$ and the elastic strain energy density function in continuum mechanics. We show that $\boldsymbol{A}$ can then be classified according to different classical elastic symmetries (i.e., isotropy, transverse isotropy, orthotropy, planar symmetry, and anisotropy). When $\boldsymbol{A}$ is an isotropic tensor, an explicit expression for $p(\boldsymbol{D})$, and for the distribution of its three eigenvalues, $p(\gamma_1,\gamma_2,\gamma_3)$, are derived, which are confirmed by Monte Carlo simulations. Sample estimates of $\boldsymbol{A}$ are also obtained using synthetic DT-MRI data. Estimates of $p(\boldsymbol{D})$ should be useful in feature extraction and in classification of noisy, discrete tensor data.

1. INTRODUCTION

Diffusion Tensor MRI (DT-MRI) [1] (that provides a measurement of a symmetric 2nd-order diffusion tensor of water, $\boldsymbol{D}$, for each voxel within an imaging volume), requires the development of a normal distribution for a tensor-valued random variable.

Although the multivariate [2] normal distribution adequately treats vector-valued random variables, the conventional way to treat a normal random variable that is a 2nd (or higher) order tensor is to write it as a vector random variable described using a multivariate normal distribution (e.g., see [3]). However, DT-MRI requires the determination not only of the distribution and moments of the individual elements of $\boldsymbol{D}$, but also of the distribution and moments of the eigenvalues and eigenvectors of $\boldsymbol{D}$ (and those of other scalar invariant quantities derived from $\boldsymbol{D}$). This information is not readily available when one writes $\boldsymbol{D}$ as a 6x1-vector [3].

Additionally, writing a tensor as vector obscures many fundamental intrinsic algebraic relationships among its elements and its geometric structure. For example, operations naturally performed on a tensor (e.g., expanding it in terms of its eigenvalues and eigenvectors, projecting it along a particular direction, or applying an affine transformation to it) all are unwieldy when it is written as a vector.

Moreover, the theory of multivariate distributions provides no means to determine the effect of an affine transformation on the distribution of $\boldsymbol{D}$, or of the distribution of its projection (i.e., of an apparent diffusion constant or ADC) along a particular direction. Finally, the covariance (or precision) matrix of this multivariate distribution provides no insight into the physical processes by which experimental noise or the experimental design affect the estimate of tensor-derived quantities.

The new *tensor*-variate normal distribution we propose preserves the geometric structure, algebraic form, and our ability to perform various tensor algebraic operations on a tensor random variable.

2. THEORY

The scalar exponent of a multivariate normal probability density function (pdf), $p(x)$, is a quadratic form, $x^T \boldsymbol{M}\, x$, of an N-dimensional normal random vector, x, and the precision (or inverse covariance) matrix, $\boldsymbol{M}$:

$$p(x) = \sqrt{\frac{|M|}{(2\pi)^N}}\, e^{-\frac{1}{2} x^T M\, x} = \sqrt{\frac{|M|}{(2\pi)^N}}\, e^{-\frac{1}{2} x_i M_{ij} x_j} \qquad (1)$$

In tensor parlance, $x^T \boldsymbol{M}\, x$ is a *scalar contraction*–a linear operation that reduces one or more higher order tensors to a 0th-order tensor (or scalar). In this case, $x_i\ M_{ij}\ x_j$ [1] above is a scalar contraction of a 2nd-order precision tensor[2], $\boldsymbol{M}$, and the 1st-order tensor, x, resulting in a linear combination of quadratic functions that are products of elements of the vector, x, such as $x_i\ x_j$, and the corresponding element of $\boldsymbol{M}$, M_{ij}.

In generalizing the multivariate normal distribution to a *tensor*-variate normal distribution, we construct a linear combination of quadratic terms that are products of the components of the tensor, $\boldsymbol{D}$, such as $D_{ij}\ D_{mn}$, and the corresponding element of a 4th-order tensor, $\boldsymbol{A}$, A_{ijmn},

$$D_{ij}\, A_{ijmn}\, D_{mn} \qquad (2)$$

Analogously, $D_{ij}\, A_{ijmn}\, D_{mn}$ is a scalar contraction of a 4th-order tensor, $\boldsymbol{A}$, and a 2nd-order tensor, $\boldsymbol{D}$. Thus, we propose a normal distribution for a 2nd-order tensor

[1] We use the Einstein summation convention in which indices that are repeated are summed over the range of their allowable values.
[2] $\boldsymbol{M}$ is usually referred to as a matrix, but it transforms as a 2nd-order tensor.

random variable, $\boldsymbol{D}$, and 4th-order precision tensor, $\boldsymbol{A}$, of the form:

$$p(D) = c\ e^{-\frac{1}{2} D_{ij} A_{ijmn} D_{mn}} \qquad (3)$$

where c is the normalization constant derived in **2.3**.

2.1. Analogies with continuum mechanics

The exponent in Eq. (3) above, $-\ 1/2\, D_{ij} A_{ijmn} D_{mn}$, has the same form as the strain energy density (e.g., see [4]) that appears in elasticity theory to describe the amount of internal energy stored in deformation. Specifically, there is a direct analogy between $\boldsymbol{D}$ and the 2nd-order strain tensor, and between $\boldsymbol{A}$ and the 4th-order tensor of elastic coefficients.

Moreover, the 4th-order precision tensor, $\boldsymbol{A}$ shares other properties with the tensor of elastic coefficients. $\boldsymbol{A}$ possesses symmetries, which leave its value unaltered by the exchange of certain pairs of indices. For example, since the product of two elements of the 2nd-order tensor commute, $D_{ij} D_{mn} = D_{mn} D_{ij}$, the corresponding coefficients of A_{ijmn} should be the same (i.e., $A_{ijmn} = A_{mnij}$) in the scalar contraction $D_{ij} A_{ijmn} D_{mn}$. Also, since $\boldsymbol{D}$ is symmetric, i.e., $D_{ij} = D_{ji}$ and $D_{mn} = D_{nm}$, we require that $A_{ijmn} = A_{jimn}$ and $A_{ijmn} = A_{ijnm}$, respectively. In continuum mechanics, these symmetries arise because the form of the strain energy function should not depend upon the coordinate system in which the components of the strain tensor are measured (e.g., see [5]). This requirement applies equally to the statistical distribution of a 2nd-order tensor.

Owing to the symmetry conditions stated above, out of 81 elements of $\boldsymbol{A}$, at most 21 independent elements must be specified *a priori* [5] or estimated.

The theory of elasticity also offers a scheme to classify the 4th-order tensor, $\boldsymbol{A}$, according to the number, types, and degrees of symmetries it possesses. The least symmetric form of $\boldsymbol{A}$, denoted by *anisotropy* or *aeolotropy*, requires all 21 constants [4]. Other symmetries include *planar symmetry*, requiring 13 elastic coefficients; *orthotropy*, requiring 9 elastic coefficients; *transverse isotropy*, requiring 5 elastic coefficients; and *isotropy*, requiring only 2 elastic coefficients. In **2.4**, we analyze in detail the case when $\boldsymbol{A}$ is isotropic.

2.2 Relationship between A and the matrix, M

Another important result from continuum mechanics, which we also exploit here, is that any 4th-order tensor, $\boldsymbol{A}$, satisfying the symmetry properties in **2.1**, can be mapped to a 6x6 symmetric tensor (matrix) $\boldsymbol{M}$ containing the same 21 independent coefficients as $\boldsymbol{A}$ (e.g., see [4, 6, 7]). We use this result to rewrite the scalar contraction, $D_{ij} A_{ijmn} D_{mn}$, as a quadratic form, $\tilde{D}_r M_{rs} \tilde{D}_s$, in which the 2nd-order symmetric tensor, $\boldsymbol{D}$, is now written as 6-d vector $\tilde{D} = \left(D_{xx}, D_{yy}, D_{zz}, 2D_{xy}, 2D_{xz}, 2D_{yz}\right)^T$. This correspondence allows us to construct a 6x6 precision matrix (tensor) $\boldsymbol{M}$, directly from a 4th-order precision tensor, $\boldsymbol{A}$.

This mapping also provides a method to construct a corresponding multivariate normal distribution directly from a tensor-variate normal distribution. We can then exploit the elaborate mathematical machinery developed for multivariate distributions to calculate the normalization constant (see Section **2.3**), likelihood function, maximum likelihood estimates of its moments, etc. of a tensor-variate normal distribution.

2.3 Normalization constant for p(D)

We obtain the normalization constant, c, of the tensor-variate normal pdf by integrating $p(\boldsymbol{D})$ from Eq. (3) over all six independent elements of the symmetric tensor, $\boldsymbol{D}$,

$$1 = \int_{-\infty}^{\infty} \ldots \int_{-\infty}^{\infty} c\, e^{-\frac{1}{2} D_{ij} A_{ijmn} D_{mn}}\, dD = c \int_{-\infty}^{\infty} \ldots \int_{-\infty}^{\infty} e^{-\frac{1}{2} D:A:D}\, dD \qquad (4)$$

Here, the tensor dot product '**:**' denotes the contraction of the 2nd-order tensor and the 4th-order precision tensor. The corresponding precision matrix, $\boldsymbol{M}$, which contains elements of the 4th-order tensor, $\boldsymbol{A}$, is given by,

$$M = \begin{pmatrix} A_{xxxx} & A_{xxyy} & A_{xxzz} & A_{xxxy} & A_{xxxz} & A_{xxyz} \\ A_{xxyy} & A_{yyyy} & A_{yyzz} & A_{yyxy} & A_{xzyy} & A_{yyyz} \\ A_{xxzz} & A_{yyzz} & A_{zzzz} & A_{xyzz} & A_{xzzz} & A_{yzzz} \\ A_{xxxy} & A_{xyyy} & A_{xyzz} & A_{xyxy} & A_{xyxz} & A_{xyyz} \\ A_{xxxz} & A_{xzyy} & A_{xzzz} & A_{xyxz} & A_{xzxz} & A_{xzyz} \\ A_{xxyz} & A_{yyyz} & A_{yzzz} & A_{xyyz} & A_{xzyz} & A_{yzyz} \end{pmatrix} = \begin{pmatrix} \Gamma & \Xi \\ \Xi^T & \Psi \end{pmatrix} \qquad (5)$$

The normalization constant is then readily obtained [8]:

$$c = \sqrt{\frac{|M|}{(2\pi)^6}} = \frac{\sqrt{|M|}}{(2\pi)^3} = \frac{\sqrt{\left|\Gamma - \Xi\Psi^{-1}\Xi^T\right| \left|\Psi\right|}}{(2\pi)^3} \qquad (6)$$

The last expression in Eq. (6) is obtained by writing $\boldsymbol{M}$ as four 3x3 block matrices, and noting that $\Gamma = \Gamma^T$ and $\Psi = \Psi^T$.

Generally, the tensor-variate distribution, $p(\boldsymbol{D})$, with precision tensor, $\boldsymbol{A}$, and mean tensor, $\boldsymbol{D}^0$, is given by:

$$p(D) = \frac{\sqrt{\left|\Gamma - \Xi\Psi^{-1}\Xi^T\right| \left|\Psi\right|}}{(2\pi)^3}\, e^{-\frac{1}{2}\left(D_{ij} - D_{ij}^0\right) A_{ijmn} \left(D_{mn} - D_{mn}^0\right)} \qquad (7)$$

This distribution possesses the form and properties of a normal distribution. Above, $\boldsymbol{D}$:$\boldsymbol{A}$:$\boldsymbol{D}$ is always non-negative since $\boldsymbol{A}$ is positive semi-definite (having six non-negative eigenvalues and six real *eigentensors* [6]). This ensures that $0 \le p(\boldsymbol{D}) < 1$ [3]. The exponent of $p(\boldsymbol{D})$ is a quadratic function of the random variable $\boldsymbol{D}$. The mean and precision tensors in Eq. (7) are analogous to the mean vector and precision matrix of the multivariate distribution.

2.4 p(D) for a 4th-order isotropic precision tensor, A

[3] In continuum mechanics this ensures elastic stability, i.e., stresses developed always return a sample to its equilibrium configuration [9].

Here we derive an explicit form of $p(\boldsymbol{D})$ for the case in which $\boldsymbol{A}$ is an isotropic 4th-order tensor. When $\boldsymbol{A}$ possesses the symmetries described in **2.1**, and also is isotropic, its most general form is (e.g., see [5, 7]):

$$A_{ikpm} = \lambda\, \delta_{ik}\, \delta_{mp} + \mu \left(\delta_{im}\, \delta_{kp} + \delta_{ip}\, \delta_{km}\right) \qquad (8)$$

where μ and λ are undetermined constants[4], and δ_{im} is a 2nd-order isotropic tensor. For $\boldsymbol{A}$ given in Eq. (8), the exponent of $p(\boldsymbol{D})$ in Eq. (7) reduces to:

$$D_{ij}\, A_{ijmn}\, D_{mn} = D : A : D = \lambda \left(Trace(D)\right)^2 + 2\,\mu\, Trace(D^2) \quad (9)$$

Since Eq. (9) is a function only of two scalar invariants of $\boldsymbol{D}$, i.e. Trace($\boldsymbol{D}$) and Trace($\boldsymbol{D}^2$), it follows that isotropy of $\boldsymbol{A}$ implies rotational invariance of $p(\boldsymbol{D})$ (i.e., $p(\boldsymbol{D})$ assumes the same form under any proper rotation of the laboratory coordinate frame of reference).

To compute properties of $p(\boldsymbol{D})$, we again write $\boldsymbol{D}$ as a vector, and write the exponent as a quadratic form, $\tilde{D}^T M\, \tilde{D}$. Then,

$$M = \begin{pmatrix} \lambda+2\mu & \lambda & \lambda & 0 & 0 & 0 \\ \lambda & \lambda+2\mu & \lambda & 0 & 0 & 0 \\ \lambda & \lambda & \lambda+2\mu & 0 & 0 & 0 \\ 0 & 0 & 0 & \mu & 0 & 0 \\ 0 & 0 & 0 & 0 & \mu & 0 \\ 0 & 0 & 0 & 0 & 0 & \mu \end{pmatrix} = \begin{pmatrix} \Gamma & \Xi \\ \Xi^T & \Psi \end{pmatrix} \qquad (10)$$

Clearly, the diagonal elements of $\boldsymbol{D}$ are mutually correlated because the block matrix, Γ, is not diagonal. However, the coupling among the diagonal elements is independent of their size. Moreover, since $\Xi=\boldsymbol{0}$, the diagonal elements and off-diagonal elements of $\boldsymbol{D}$ are uncorrelated. Finally, the off-diagonal elements of $\boldsymbol{D}$ are themselves independently distributed since $\Psi=\mu\, \boldsymbol{I}$ (where $\boldsymbol{I}$ is the identity tensor). Thus, $p(\boldsymbol{D})$ simplifies to:

$$p(D) = p(D_{xx}, D_{yy}, D_{zz})\; p(D_{xy})\, p(D_{xz})\, p(D_{yz}) \qquad (11)$$

where

$$p(D_{xx}, D_{yy}, D_{zz}) = \sqrt{\frac{4\mu^2(2\mu+3\lambda)}{(2\pi)^3}}\; e^{-\frac{1}{2}\left(D_{xx},\, D_{yy},\, D_{zz}\right)\begin{pmatrix} 2\mu+\lambda & \lambda & \lambda \\ \lambda & 2\mu+\lambda & \lambda \\ \lambda & \lambda & 2\mu+\lambda \end{pmatrix}\begin{pmatrix} D_{xx} \\ D_{yy} \\ D_{zz} \end{pmatrix}}$$

$$p(D_{xy}) = \sqrt{\frac{\mu}{2\pi}}\, e^{-\frac{\mu}{2} D_{xy}{}^2};\ p(D_{xz}) = \sqrt{\frac{\mu}{2\pi}}\, e^{-\frac{\mu}{2} D_{xz}{}^2};\ p(D_{yz}) = \sqrt{\frac{\mu}{2\pi}}\, e^{-\frac{\mu}{2} D_{yz}{}^2} \qquad (12)$$

One substantive difference between tensor-variate and multivariate normal distributions is the way in which their covariance structures are characterized. Although $\boldsymbol{A}$ is an isotropic precision tensor, $\boldsymbol{M}$ in Eq. (10) is clearly not an isotropic precision matrix (or tensor). In fact, $\boldsymbol{M}$ is not even diagonal. Only for $\lambda=0$, when all elements of $\boldsymbol{D}$ are independently distributed, is $\boldsymbol{M}$ a diagonal matrix. Even then, $\boldsymbol{M}$ is still not isotropic. Thus, even for an isotropic 4th-order precision tensor the relationship between the tensor-variate and multivariate normal distributions is not trivial. Clearly, $\boldsymbol{A}$ represents a new covariance structure.

[4] λ and μ are the Lamé constant and shear modulus, respectively [9].

2.5 Distribution of eigenvalues of *D*, $p(\gamma_1,\gamma_2,\gamma_3)$, for a 4th-order isotropic precision tensor, *A*

For a 4th-order isotropic precision tensor, $\boldsymbol{A}$, we can obtain $p(\gamma_1,\gamma_2,\gamma_3)$, the joint pdf of the three eigenvalues of $\boldsymbol{D}$, directly from Eq. (9) by substituting $Trace(D) = \gamma_1 + \gamma_2 + \gamma_3$ and $Trace\left(D^2\right) = \gamma_1^2 + \gamma_2^2 + \gamma_3^2$ and collecting terms:

$$p(\gamma_1,\gamma_2,\gamma_3) = \sqrt{\frac{4\mu^2(2\mu+3\lambda)}{(2\pi)^3}}\; e^{-\frac{1}{2}\left(\gamma_1,\, \gamma_2,\, \gamma_3\right)\begin{pmatrix} 2\mu+\lambda & \lambda & \lambda \\ \lambda & 2\mu+\lambda & \lambda \\ \lambda & \lambda & 2\mu+\lambda \end{pmatrix}\begin{pmatrix} \gamma_1 \\ \gamma_2 \\ \gamma_3 \end{pmatrix}} \qquad (13)$$

The covariance matrix of $p(\gamma_1,\gamma_2,\gamma_3)$ depends only on μ and λ. While the eigenvalues are correlated, their coupling is independent of how they are ordered; permuting them leaves $p(\gamma_1,\gamma_2,\gamma_3)$ unchanged. This follows from the fact that the scalar invariants of $\boldsymbol{D}$, Trace($\boldsymbol{D}^2$) and Trace($\boldsymbol{D}$)^2, are inherently insensitive to how the eigenvalues are assigned.

We then uncorrelate or whiten $p(\gamma_1,\gamma_2,\gamma_3)$ by diagonalizing the precision matrix [8] in Eq. (13). The covariance matrix for this new distribution is:

$$\Sigma = \begin{pmatrix} \frac{1}{2\mu+3\lambda} & 0 & 0 \\ 0 & \frac{1}{2\mu} & 0 \\ 0 & 0 & \frac{1}{2\mu} \end{pmatrix} = \begin{pmatrix} \sigma_T^2 & 0 & 0 \\ 0 & \sigma_S^2 & 0 \\ 0 & 0 & \sigma_S^2 \end{pmatrix} \qquad (14)$$

2.6 Monte Carlo simulations of $p(\gamma_1,\gamma_2,\gamma_3)$ for the isotropic tensor, *A*.

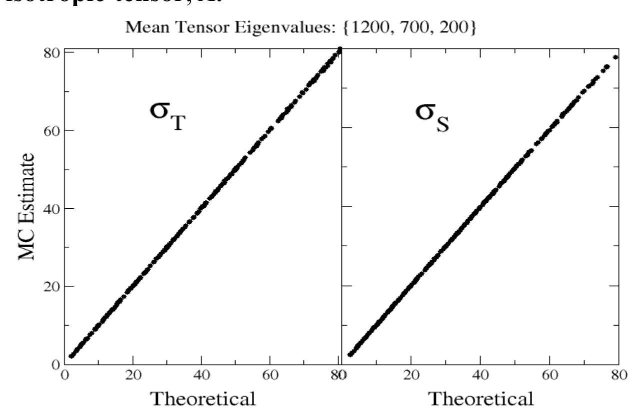

Figure 1. 300 points from MC simulations of 2nd-order tensor, $\boldsymbol{D}$, with $(\gamma_1,\gamma_2,\gamma_3)$ = (1200, 700, 200), typical of brain white matter. The precision of MC estimates was 0.2%.

In Figure 1, we plot Monte Carlo (MC) estimates of σ_T and σ_S against their theoretical values obtained from Eq. (14). First, MC estimates of $\boldsymbol{D}$ are generated from the multivariate normal distribution with precision matrix given Eq. (10). Then, the empirical distribution, $p(\gamma_1, \gamma_2, \gamma_3)$, is computed using these $\boldsymbol{D}$. Agreement is excellent. Values of μ and λ are chosen randomly but so that the distributions of distinct eigenvalues do not overlap to avoid a known "sorting" bias that would produce erroneous estimates of σ_T and σ_S.

2.7 Estimating *A* from simulated DT-MR experiments

MC simulations were also performed to generate $\boldsymbol{A}$ from diffusion tensors, $\boldsymbol{D}$, typical of those measured in human brain with DT-MRI. Using experimental parameters provided in [10], we synthesize DT-MR data using MC methods as described in [11]. From the empirically estimated $\boldsymbol{D}$ values, we obtained sample estimates of $\boldsymbol{A}$ for a putative gray matter region. Figure 2 shows $\boldsymbol{A}$ displayed as a 6x6 matrix with coefficients organized as in Eq. (5).

Classifying the symmetries of these estimated 4th-order tensors is assessed using an eigenvalue-eigentensor decomposition. For an isotropic $\boldsymbol{D}$ tensor corresponding to brain gray matter, the symmetry shown in Figure 2 is characterized by only three independent parameters. This makes the estimated $\boldsymbol{A}$ only slightly more complicated than the 2-parameter isotropic model considered above, but less complicated than the 5-parameter transverse isotropic model. A hypothesis that we are currently testing is that one objective of an optimal experimental design is to make $\boldsymbol{A}$ closest to being isotropic.

$$\begin{pmatrix} 56 & 7 & 7 & 0 & 0 & 0 \\ 7 & 56 & 7 & 0 & 0 & 0 \\ 7 & 7 & 56 & 0 & 0 & 0 \\ 0 & 0 & 0 & 49 & 0 & 0 \\ 0 & 0 & 0 & 0 & 49 & 0 \\ 0 & 0 & 0 & 0 & 0 & 49 \end{pmatrix} = \begin{pmatrix} a & c & c & 0 & 0 & 0 \\ c & a & c & 0 & 0 & 0 \\ c & c & a & 0 & 0 & 0 \\ 0 & 0 & 0 & b & 0 & 0 \\ 0 & 0 & 0 & 0 & b & 0 \\ 0 & 0 & 0 & 0 & 0 & b \end{pmatrix}$$

Figure 2. Elements of $\boldsymbol{A}$ (as organized in Eq. (5)) estimated from MC simulations of $\boldsymbol{D}$ using gray matter parameters $(\gamma_1, \gamma_2, \gamma_3)$ = (700, 700, 700) at SNR = 10. The general form of $\boldsymbol{A}$ is given using the three parameters a, b, and c, above.

3. DISCUSSION

This new tensor-variate distribution should improve our estimates of $\boldsymbol{D}$ and quantities derived from it in DT-MRI [12, 13], and lead to the development of new hypothesis tests to analyze DT-MRI data as well as to improvements in experimental design.

New methods are being developed to measure other tensor quantities, such as rotational or spin-diffusion tensors, and tensors of elastic coefficients [14]. Tensors that characterize charge, mass, momentum, and energy transport are also of great importance in material sciences, physics, and medicine. In addition to the translational diffusion tensor measured by DT-MRI, these include the dispersion, electrical conductivity, thermal conductivity, and hydraulic permeability tensors. These quantities may conform to a normal tensor-variate distribution, especially if measured using regression methods (e.g., as in [15]).

4. CONCLUDING REMARKS

The use of a scalar contraction of 4th- and 2nd-order tensors in the exponent of a normal distribution appears to be a novel development in the theory of statistical distributions, and significantly extends the scope and range of applicability of the normal distribution to accommodate higher dimensional data structures.

Using a 4th-order tensor to characterize the covariance structure of the tensor-variate distribution preserves the form of the tensor random variable, and our ability to perform admissible algebraic operations on it. It also provides a way to assess the type and degrees of symmetry in the correlations between components of the random tensor, obscured when these components are described by a multivariate normal distribution.

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